Assessment of the severity of acute pulmonary embolism using CT pulmonary angiography parameters

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Aim. To evaluate the association between computed tomography parameters and clinical signs in patients with acute pulmonary embolism.

Methods. 109 patients retrospectively selected from hospital database with acute pulmonary embolism verified by CT pulmonary angiography. The following parameters were assessed: pulmonary artery diameter to aorta diameter ratio (PA/Ao), normalized pulmonary artery diameter (nPA), right ventricular to left ventricular diameter ratio from CT (RV CT/LV CT), normalized end-diastolic right ventricular diameter (nRVD echo) and right to left ventricular end diastolic diameter ratio (RV echo/LV echo) from echocardiography.

Results. Multivariate regression analysis showed a significant association between PA/Ao and thrombolysed (0.99) to non-thrombolysed (0.90) patients, OR=1.56 $P=0.012$, and also RV CT/LV CT and thrombolysed 1.5 to non-thrombolysed (0.94) patients OR=1.24 $P=0.002$. The significant difference was also found in intensive care unit hospitalization necessity (ICU-Y/N) and RV CT/LV CT ratio (ICU-Y 1.42, ICU-N 0.91) OR=1.26 $P=0.003$, and RV echo/LV echo (ICU-Y 0.82, ICU-N 0.65) OR=1.83 $P=0.033$.

Conclusion. From the CT pulmonary angiography parameters, the RV CT/LV CT showed a significant association with both thrombolysis administration and ICU hospitalization. The PA/Ao had relation only to thrombolytic therapy as well as RV echo/LV echo only to ICU hospitalization.

Key words: pulmonary embolism, risk assessment, CT angiography, clinical signs

Received: January 18, 2013; Accepted with revision: October 22, 2013; Available online: November 8, 2013
<http://dx.doi.org/10.5507/bp.2013.082>

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INTRODUCTION

Acute pulmonary embolism (PE) is one of the most frequent cardiovascular conditions. The incidence in Europe is about 50 cases/100000 inhabitants according to data from the European Society of Cardiology¹. The mortality rate of acute pulmonary embolism is about 30% in non-treated patients and about 8% in treated patients. Approximately 11% of patients die of sudden death². A number of risk factors have been identified: age over 70 years, congestive heart failure and other cardiopulmonary diseases^{3,4}. Echocardiographic findings^{4,5} as right ventricular (RV) dysfunction (assessed as hypokinesis of RV free wall, or dilatation of right ventricle compared to left ventricle) and laboratory markers as troponin T (ref.⁶⁻⁸) and NT-proBNP (ref.⁹⁻¹¹) are also associated with poor prognosis. One of the first examination techniques in patients with acute pulmonary embolism is CT pulmonary angiography (pCTA) and there are several studies demonstrating the importance of pCTA in patients suspected of having PE (ref.¹²). In previous studies these parameters were mainly analyzed: pulmonary artery/aorta ratio, right ventricular/left ventricular ratio, pulmonary obstruction index (POI), ventricular septal bowing (VSB) and venous contrast reflux (VCR) (ref.¹²⁻¹⁵). In our study, we used pulmonary artery normalized diameter (nPA), PA/Ao ratio,

RV CT/LV CT ratio in comparison with echocardiography parameters – normalized right ventricular diastolic diameter (nRV echo) and RV/LV diastolic diameter ratio (RVecho/LV echo).

PATIENTS AND METHODS

Patients hospitalized from August 2007 through May 2012 were retrospectively selected from the hospital information system. Patients with ejection fraction under 50% on echocardiography, chronic pulmonary disease in anamnesis and a recidive of PE were excluded. A total of 109 patients with pCTA confirmed pulmonary embolism were included in the study. Patients were divided according to following criteria: clinical haemodynamical signs (hypotension, defined as systolic blood pressure under 100 mmHg or tachycardia over 100 beats per minute on admission), laboratory markers (NT-pro BNP, troponin T), clinical outcome (thrombolysed /non-thrombolysed patients and the need for intensive care unit hospitalization).

CT pulmonary angiography and echocardiography

All patients were examined on a 64 row detector system (Lightspeed VCT, GE Healthcare, Waukesha,

Fig. 1. Measurement of aorta and pulmonary artery diameter.

Fig. 2. Measurement of right and left ventricular diameter.

Wisconsin, USA). The examination was performed in supine position with both arms extended above the head. The following scan parameters were used: 120 kV, 700 mA, pitch 1:0.984 and 0.625 mm reconstruction slice thickness. Contrast enhancement was achieved with 100 mL of non-ionic contrast injected at 4 mL/s. Pulmonary

embolism was confirmed in all patients by an experienced radiologist. CT measurements were performed by a single reviewer (cardiologist), in eighteen patients the measurements were repeated by another cardiologist to assess the interobserver variability. The aortic and pulmonary artery diameter were measured at the short axis distance at the position where the pulmonary artery trunk and bifurcation were seen (Fig. 1). LV and RV diameter were measured at mitral valve plane and tricuspid valve level respectively (Fig. 2). Right and left diastolic diameter were assessed from echocardiographic measurements.

Table 1a. Outcome variables.

Parameter	N (%)
Hypotension	6 (5.5%)
Tachycardia	47 (43.1%)
Hypotension and/or tachycardia	48 (44.0%)
Trombolysis	32 (29.4%)
Intensive care unit hospitalization	59 (54.1%)
Death	2 (1.8%)

Statistical analysis

Patients were divided according to the following criteria into dichotomous groups: clinical hemodynamical signs (with hypotension and/or tachycardia on admission vs without); laboratory markers (with value of NT-pro

Table 1b. Basic characteristic of patients – continuous variables.

Parameter	N/missing	Mean (SD)	Median	All patients (N=109)	
				Lower quartile-Upper quartile	Min-Max
Age (years)	109/0	61.99 (16.20)	64.00	54.00 - 73.00	21.0 - 90.0
Body mass index (kg/m ²)	109/0	29.16 (5.92)	28.33	25.34 - 31.77	18.0 - 50.8
BSA (m ²)	109/0	2.05 (0.82)	1.97	1.81 - 2.10	1.5 - 10.2
Hospitalization (days)	98/11	10.91 (14.24)	8.00	7.00 - 11.00	2.0 - 120.0
Intensive care unit hospitalization (days)	109/0	2.90 (6.35)	2.00	0.00 - 4.00	0.0 - 60.0
NT proBNP (ng/L)	43/66	4016.55 (5351.58)	2352.00	493.00 - 4483.00	32.0 - 22553.0
Troponin T (ng/L)	47/62	0.07 (0.14)	0.03	0.01 - 0.10	0.0 - 1.0
PA/Ao	109/0	0.94 (0.16)	0.94	0.83 - 1.03	0.6 - 1.5
nPA	109/0	14.97 (2.57)	14.80	13.00 - 16.30	10.2 - 22.8
RV CT/LV CT	109/0	1.25 (0.49)	1.14	0.89 - 1.50	0.5 - 2.9
nRV echo	109/0	16.77 (3.30)	16.02	14.71 - 18.42	10.7 - 27.3
RV echo/LV echo	109/0	0.77 (0.23)	0.73	0.61 - 0.87	0.4 - 1.8
SBP in RV (estimate)	83/26	41.25 (15.89)	40.00	30.00 - 50.00	20.0 - 100.0

PA - pulmonary artery, Ao - aorta, BSA - body surface area, RV - right ventricle, LV - left ventricle, SBP - systolic blood pressure, NT-pro BNP - N-terminal pro-B-type natriuretic peptide

Table 2. Patients with and without clinical haemodynamical signs in admission.

Parameter	Patients with hypotension and/or tachycardia (N=48)	Patients without hypotension and tachycardia (N=61)	<i>P</i> *	Univariate logistic regression		Multivariate logistic regression	
				<i>P</i>	Odds ratio (95% confidence interval)**	<i>P</i>	Odds ratio (95% confidence interval)**
PA/Ao	0.96 (0.87 - 1.03)	0.91 (0.82 - 1.03)	0.163	0.154	1.20 (0.94 - 1.53)	0.501	1.11 (0.82 - 1.51)
nPA	15.25 (13.70 - 16.65)	14.40 (12.70 - 16.00)	0.150	0.100	1.14 (0.98 - 1.32)	0.872	0.98 (0.80 - 1.21)
RV CT/LV CT	1.41 (0.99 - 1.75)	0.94 (0.82 - 1.23)	<.001	<.001	1.20 (1.09 - 1.33)	0.129	1.10 (0.97 - 1.24)
nRV echo	17.93 (15.53 - 19.83)	15.57 (14.21 - 17.00)	<.001	0.001	1.26 (1.10 - 1.45)	0.644	0.94 (0.71 - 1.23)
RV echo/LV echo	0.86 (0.75 - 1.00)	0.67 (0.59 - 0.75)	<.001	<.001	1.65 (1.27 - 2.13)	0.062	1.56 (0.98 - 2.49)

PA - pulmonary artery, Ao - aorta, BSA - body surface area, RV - right ventricle, LV - left ventricle

Median (lower quartile-upper quartile) are presented.

* Wilcoxon two sample test for comparison of differences between groups of patients

** *P*-value of Wald test and odds ratio for patients with hypotension and/or tachycardia

For the parameters PA/Ao, RV CT/LV CT and RV echo/LV echo unit 0.1 was used in order to present odds for hypotension and/or tachycardia if the value of parameters is increased by 0.1. For parameters PA/BSA and RV echo index unit 1 was used.

Table 3. Patients thrombolysed or non-thrombolysed.

Parameter	Trombolysed patients (N=32)		Non-trombolysed patients (N=77)		<i>P</i> *	Univariate logistic regression		Multivariate logistic regression	
						<i>P</i>	Odds ratio (95% confidence interval)**	<i>P</i>	Odds ratio (95% confidence interval)**
PA/Ao	0.99	(0.91 - 1.10)	0.90	(0.81 - 1.00)	0.005	0.004	1.51 (1.14 - 2.01)	0.012	1.56 (1.10 - 2.21)
nPA	15.60	(13.80 - 16.95)	14.50	(12.50 - 16.00)	0.049	0.098	1.15 (0.97 - 1.35)	0.283	0.88 (0.69 - 1.12)
RV CT/LV CT	1.50	(1.28 - 1.79)	0.94	(0.82 - 1.27)	<.001	<.001	1.26 (1.13 - 1.41)	0.002	1.24 (1.08 - 1.43)
nRV echo	18.38	(16.04 - 20.20)	15.68	(14.35 - 17.76)	<.001	0.003	1.23 (1.07 - 1.40)	0.360	1.16 (0.84 - 1.60)
RV echo/LV echo	0.84	(0.76 - 1.00)	0.68	(0.60 - 0.81)	<.001	0.006	1.35 (1.09 - 1.66)	0.559	0.88 (0.58 - 1.34)

PA - pulmonary artery, Ao - aorta, BSA - body surface area, RV - right ventricle, LV - left ventricle

Median (lower quartile-upper quartile) are presented.

* Wilcoxon two sample test for comparison of differences between groups of patients

** *P*-value of Wald test and odds ratio for thrombolysed patients

For the parameters PA/Ao, RV CT/LV CT and RV echo/LV echo unit 0.1 was used in order to present odds for thrombolysed patients if the value of parameters is increased by 0.1. For parameters PA/BSA and RV echo index unit 1 was used.

BNP > 1000 ng/L vs ≤ 1000 ng/L; with value of troponin T > 0.09 µg/L vs ≤ 0.09 µg/L); clinical outcome (thrombolysed vs non-thrombolysed patients; needing intensive care unit hospitalization vs without; intensive care unit hospitalization ≥ 4 days vs < 4 days). Because the assumption of normal distribution was remarkably violated for most continuous parameters (Shapiro-Wilk's test), median, lower quartile (Q1) and upper quartile (Q3) were used for the presentation of data and non-parametric Mann-Whitney tests were conducted for the comparison of groups. Univariate and multivariate logistic regression were used to determine predictors and independent predictors of each criterion, where *p*-values are presented together with the Odds Ratios (OR) and their 95% confidence intervals. Various multivariate models were used to explore the predictive power of the tested parameters. Age, sex and BMI were used to adjust the results but this did not improve the models presented. Results with *P*-value < 0.05 are considered statistically significant.

RESULTS

A total of 109 patients were included. Fifty-one patients (47%) were male. Mean age was 62 years (21-90 years). Fifty-nine patients (54%) were hospitalized in the intensive care unit, 32 patients (29%) received thrombolytic therapy. Two patients died during hospitalization and 48 (44%) had signs of altered haemodynamics (hypotension or tachycardia) on admission. Tables 1a and 1b display findings from CT pulmonary angiography, echocardiography and laboratory measurements as well as basic patients characteristics.

Haemodynamical signs on admission

Table 2 shows the association of CT and echocardiography parameters with hypotension and/or tachycardia as presenting on admission. In univariate logistic regression analysis, the RV CT/RV CT, nRVD echo and RVD echo/LVD echo showed significant association with haemody-

Table 4. Patients with and without positive values of troponin T.

Parameter	Patients with troponin T > 0.09 µg/L (N=13)		Patients with troponin T ≤ 0.09 µg/L (N=34)	P*	Univariate logistic regression		Multivariate logistic regression		
					P	Odds ratio (95% confidence interval)**	P	Odds ratio (95% confidence interval)**	
PA/Ao	0.96	(0.91 - 1.03)	0.94	(0.87 - 1.03)	0.803	0.890	1.03 (0.69 - 1.54)	0.500	0.81 (0.44 - 1.49)
nPA	16.70	(14.60 - 17.70)	15.20	(13.50 - 15.90)	0.147	0.190	1.18 (0.92 - 1.52)	0.712	1.07 (0.74 - 1.56)
RV CT/LV CT	1.50	(1.29 - 1.70)	1.05	(0.89 - 1.44)	0.020	0.037	1.17 (1.01 - 1.36)	0.330	1.10 (0.91 - 1.34)
nRV echo	19.76	(18.23 - 21.71)	15.78	(14.69 - 18.42)	0.004	0.008	1.39 (1.09 - 1.78)	0.222	1.33 (0.84 - 2.08)
RV echo/LV echo	0.92	(0.79 - 0.95)	0.75	(0.60 - 0.88)	0.017	0.043	1.49 (1.01 - 2.20)	0.851	0.94 (0.52 - 1.72)

PA - pulmonary artery, Ao - aorta, BSA - body surface area, RV - right ventricle, LV - left ventricle

Median (lower quartile-upper quartile) are presented.

* Wilcoxon two sample test for comparison of differences between groups of patients

** P-value of Wald test and odds ratio for patients with troponin T > 0.09 µg/L

For the parameters PA/Ao, RV CT/LV CT and RV echo/LV echo unit 0.1 was used in order to present odds for troponin T > 0.09 µg/L if the value of parameters is increased by 0.1. For parameters PA/BSA and RV echo index unit 1 was used.

Table 5. Patients with and without positive values of NT-pro BNP.

Parameter	Patients with NT-pro BNP > 1000 ng/L (N=29)		P*	Univariate logistic regression		Multivariate logistic regression	
	Patients with NT-pro BNP =< 1000 ng/L (N=14)			P	Odds ratio (95% confidence interval)**	P	Odds ratio (95% confidence interval)**
PA/Ao	1.00	(0.94 - 1.08)	0.014	0.038	1.83 (1.04 - 3.24)	0.567	0.77 (0.31 - 1.90)
nPA	15.80	(14.80 - 17.60)	0.006	0.012	1.69 (1.12 - 2.54)	0.059	4.39 (0.95 - 20.43)
RV CT/LV CT	1.44	(1.16 - 1.75)	<.001	0.003	1.50 (1.14 - 1.96)	0.058	2.21 (0.97 - 5.02)
nRV echo	17.99	(15.94 - 20.18)	<.001	0.004	1.72 (1.19 - 2.48)	0.557	0.74 (0.27 - 2.03)
RV echo/LV echo	0.83	(0.76 - 0.95)	<.001	0.001	3.12 (1.56 - 6.25)	0.298	2.41 (0.46 - 12.55)

PA - pulmonary artery, Ao - aorta, BSA - body surface area, RV - right ventricle, LV - left ventricle

Median (lower quartile-upper quartile) are presented.

* Wilcoxon two sample test for comparison of differences between groups of patients

** P-value of Wald test and odds ratio for patients with NT-pro BNP > 1000 ng/L

For the parameters PA/Ao, RV CT/LV CT and RV echo/LV echo unit 0.1 was used in order to present odds for NT-pro BNP > 1000 ng/L if the value of parameters is increased by 0.1. For parameters PA/BSA and RV echo index unit 1 was used.

Table 6. Patients with and without necessity of intensive care unit hospitalization.

Parameter	Patients with necessity of intensive care unit hospitalization (N=59)	Patients without necessity of intensive care unit hospitalization (N=50)	Univariate logistic regression		Multivariate logistic regression	
			P	Odds ratio (95% confidence interval)**	P	Odds ratio (95% confidence interval)**
PA/Ao	0.95 (0.86 - 1.03)	0.89 (0.82 - 1.00)	0.152	1.20 (0.94 - 1.54)	0.926	0.98 (0.70 - 1.38)
nPA	15.20 (13.80 - 16.70)	14.15 (12.30 - 15.90)	0.016	1.22 (1.04 - 1.44)	0.357	1.11 (0.89 - 1.39)
RV CT/LV CT	1.42 (1.13 - 1.75)	0.91 (0.79 - 1.14)	<.001	1.37 (1.19 - 1.57)	0.003	1.26 (1.08 - 1.47)
nRV echo	17.73 (15.53 - 19.76)	15.23 (14.21 - 16.96)	0.001	1.27 (1.10 - 1.48)	0.149	0.80 (0.58 - 1.09)
RV echo/LV echo	0.82 (0.70 - 1.00)	0.65 (0.58 - 0.73)	<.001	1.84 (1.37 - 2.46)	0.033	1.83 (1.05 - 3.18)

PA - pulmonary artery, Ao - aorta, BSA - body surface area, RV - right ventricle, LV - left ventricle
Median (lower quartile-upper quartile) are presented.

* Wilcoxon two sample test for comparison of differences between groups of patients

** p-value of Wald test and odds ratio for patients with necessity of intensive care unit hospitalization

For the parameters PA/Ao, RV CT/LV CT and RV echo/LV echo unit 0.1 was used in order to present odds for necessity of intensive care unit hospitalization if the value of parameters is increased by 0.1. For parameters PA/BSA and RV echo index unit 1 was used.

namical signs, whereas in multivariate logistic regression none of the parameters were significant.

Therapy with fibrinolytics

The use of systemic thrombolysis from the univariate logistic regression was significantly related to PA/Ao ratio, RV CT/LV CT, nRV echo and RV echo/LV echo. Only PA/Ao ratio, RV CT/LV CT were confirmed as independent predictors from the multivariate analysis (Table 3).

Increased troponin T and NT-proBNP levels

Troponin-T above 0.09 µg/L from the univariate logistic regression was significantly associated with RV CT/LV CT, normalized RV diastolic diameter and RV/LV diastolic diameter ratio. For NT-proBNP, all CT and echo parameters presented significant association in univariate analysis. None of the parameters were significant from the multivariate analysis for troponin T or for NT-proBNP (Table 4 and 5).

Necessity for ICU treatment

Table 6 displays the association of examined parameters and necessity for ICU hospitalization. The univariate analysis showed statistically significant results for nPAD, RV CT/LV CT, nRVD echo and RV echo/LV echo. In the multivariate analysis, only RV CT/LV CT and RV echo/LV echo were determined as independent predictors.

The mean intraobserver relative changes of measurements were 1.94% for Ao diameter, 0.03% for PA diameter, 4.58% for RV CT and 1.58% for LV CT. Interobserver measurements showed following variations: Ao 3.74%, PA 1.67%, RV CT 4.8% and LV CT 3.86%.

DISCUSSION

Multidetector CT pulmonary angiography is currently probably the most frequently used imaging technique for the diagnostics of acute pulmonary embolism^{15,16}. The assessment of severity of pulmonary embolism by CT pulmonary angiography has been studied for several years, and scores for pulmonary vessel obstruction have been developed^{17,18}. Some studies found a significant relation between pulmonary clot score and mortality^{19,20} but the others did not^{15,18,21}. These findings suggest that not only pulmonary obstruction score but mainly subsequent right ventricular dysfunction determines the clinical outcome in patients with acute pulmonary embolism. Obstruction of pulmonary vessels more than 30% leads to acute pulmonary hypertension and sudden increase in right ventricular afterload. This may cause RV dilatation, hypokinesis and progression to RV failure. In severe cases, low right ventricular output results in systemic hypotension and circulation collapse²². In our study, we found a significant association of pulmonary artery to aorta ratio and right to left ventricular diameter ratio measured from CT images with using thrombolysis. The RV CT/LV CT and right to left diastolic diameter ratio (obtained from echocardiography) were also related to need for intensive care unit hospitalization. However, in multivariate analysis neither

echocardiography nor CT parameters showed significant association with hypotension and/or tachycardia or blood biomarker levels. Heyer et al.¹⁵ found that acute pulmonary embolism can lead to increase in the RV CT/LV CT ratio. In a sample of 152 patients they measured a wide range 0.5 to 3.1 and the RV CT/LV CT ratio was also the only parameter to show a significant correlation with mortality in multivariate regression analysis. This is in accordance with our results (range of RV CT/LV CT was 0.5 to 2.9), but due to the small number of dead patients, it was not possible to statistically assess this. Probably it is caused by the fact that, most patients who died of acute pulmonary embolism were in poor clinical condition and died before the CT exam was done. This is the reason why we used the necessity for thrombolysis as one of the main clinical outcomes. On the other hand, some studies found no significant association between RV CT/LV CT ratio²³, or showed that the result depends on technique used – transverse versus four-chamber sections²⁴. The PA/Ao ratio showed a significant association with the administration of thrombolysis in our study. This result remains controversial, because Heyer et al.¹⁵ and van den Meer et al.²⁰ found no significant relation of this parameter to clinical conditions. In our study, we also tried to use pulmonary artery diameter normalized on body surface area, but there were no significant results from the multivariate analysis. The echocardiographic signs of right ventricular dysfunction as ventricular septal bowing (VSB) can also be assessed on CT, but in pulmonary CT angiography is VSB often overestimated due to mistake for septal flattening¹⁵. This can be improved using three-dimensional reconstructed images and ECG-triggering of scan acquisition to reduce motion artifacts. On the other hand, it leads to higher radiation dose and is time consuming. Our study has several limitations. First, it is a retrospective analysis, so the data are often incomplete and can not comprise more parameters than we analyzed. Another limitation is using axial views, which can overestimate RV diameter in comparison with the four chamber views^{25,26}. We also could not assess VSB as this depends on the phase of the cardiac cycle and the results are unconvincing in a non ECG-gated CT. The third limitation is relatively small number of patients. Another study, particularly a prospective is needed to confirm the accuracy of CT parameters and mainly to set the cut-off values to determine high risk patients.

CONCLUSION

In conclusion, in accordance with other studies, our results showed that the RV CT/LV CT ratio, in particular, is significantly associated with clinical outcome – thrombolysis and ICU hospitalization necessity. It is a fast and promising parameter for risk assessment in patients with acute pulmonary embolism.

ACKNOWLEDGEMENT

This study was supported by a European Regional Development Fund – Project FNUSA-ICRC (No. CZ.1.05/1.1.00/02.0123).

Author contributions: VK: study design, literature search, data collection, measurement of parameters, figures; RP: echocardiography examinations, measurement of parameters; VF: computed tomography examinations; RŠ: statistical analysis.

Conflict of interest statement: None declared.

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